

## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference  M0925/7069WO	<b>FOR FURTHER ACTION</b>		See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No.  PCT/US99/15816	International filing date (day/month/year)  13/07/1999	Priority date (day/month/year)  13/07/1998	
International Patent Classification (IPC) or national classification and IPC  C07B53/00			
Applicant  MASSACHUSETTS INSTITUTE OF TECHNOLOGY et al.			
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 7 sheets, including this cover sheet.</p> <p><input checked="" type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of 8 sheets.</p>			
<p>3. This report contains indications relating to the following items:</p> <ul style="list-style-type: none"> <li>I    <input checked="" type="checkbox"/> Basis of the report</li> <li>II   <input type="checkbox"/> Priority</li> <li>III   <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</li> <li>IV   <input type="checkbox"/> Lack of unity of invention</li> <li>V   <input checked="" type="checkbox"/> Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</li> <li>VI   <input type="checkbox"/> Certain documents cited</li> <li>VII   <input type="checkbox"/> Certain defects in the international application</li> <li>VIII   <input checked="" type="checkbox"/> Certain observations on the international application</li> </ul>			

Date of submission of the demand  13/01/2000	Date of completion of this report  26.09.2000
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## **INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

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## I. Basis of the report

1. This report has been drawn on the basis of (substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments.):

**Description, pages:**

1-56 as originally filed

**Claims, No.:**

15 (part),16-58, as originally filed  
59 (part),88-90

1-14,15 (part),59 (part),  
with letter of  
60-87 as received on  
14/07/2000 19/07/2000

### **Drawings, sheets:**

1/16-16/16 as originally filed

- 2. The amendments have resulted in the cancellation of:**

the description, pages:  
 the claims, Nos.: 2,8  
 the drawings, sheets:

3.  This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

- 4. Additional observations, if necessary:**

### **III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

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- the entire international application.
- claims Nos. 40-55,67-76,78-90.

because:

- the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

- the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 40-55,67-76,78-90 are so unclear that no meaningful opinion could be formed (*specify*):

**see separate sheet**

- the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- no international search report has been established for the said claims Nos. .

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

**1. Statement**

Novelty (N)	Yes:	Claims 1,3-7, 9-39,56-66,77
	No:	Claims
Inventive step (IS)	Yes:	Claims
	No:	Claims 1,3-7,9-39,56-66,77

Industrial applicability (IA)

Yes:	Claims 1,3-7,9-39,56-66,77
No:	Claims

**2. Citations and explanations**

**see separate sheet**

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**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

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- D1 O. Fujimura et al., J. Org. Chem., 63(3), 1998, 824-832
- D2 J. B. Alexander et al., J. Am. Chem. Soc., 120(16), 1998, 4041-4042
- D3 O. Fujimura et al., J. Am. Chem. Soc., 118(10), 1996, 2499-2500, cited by the applicant
- D4 L. E. Martinez et al., J. Am. Chem. Soc., 117(21), 1995, 5897-5898
- D5 WO 99 42469
- D6 D. S. La et al., J. Am. Chem. Soc.,120(37), 1998, 9720-9721

**Item III**

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The definition of the substrate used in claim 80 is vague, "association" of an olefin group with a ring structure, rendering the extent of protection sought in this claim unclear (Article 6 PCT). It was assumed this definition to be illustrated by the compound 14 (table 2, page 9721) of D6.
2. The subject-matters of claims 40-55, 67-76, 78-90 are defined in terms of the result to be achieved, contravening to the requirements of Article 6 PCT. These are accordingly superfluous and should be deleted.

**Item V**

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

The priority of the present demand could not be checked. If it were to be invalid, D6 (pg 9720, compounds 1a and 1b, Scheme 1; table 2 and equation(1)) would be considered as pertinent when the present application enters the national phase (Article 33(1) PCT).

**1. Amendments - Article 34(2)b PCT**

In order to overcome the novelty/clarity objection of the written opinion dated on the 14.07.2000, the applicant modified the original set of claims. Such amendment do not introduce new subject-matter which extends beyond the content of the application as originally filed. They are allowable, Article 34(2)b PCT.

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**2. Novelty and inventive step**

Examination was pursued in light of the examples.

The present application (claim 77) can be seen as a catalytic kinetic resolution and enantioselective desymmetrization through ring-closing metathesis reaction on a molecular substrate with a plane of symmetry using a chiral biphen-Mo complex in an amount of less than 15 mol% relative to an amount of substrate with or without solvent in order to recover one enantiomer in at least 50% ee. No disclosure in D1-D5 could be found to object to the novelty of claims 1, 3-7, 9-39, 56-66 and 77 (Article 33(2) PCT).

D1, which is considered as the closest prior art, pertains to an asymmetric ring-closing metathesis reaction using a Mo complex in 50% mol amount on a substrate with a plane of symmetry (page 828, equation (4)). The chiral biphen-Mo complex as defined in claim 84 of the present demand is already known from D2 for catalytic enantioselective ring-closing metathesis and for kinetic resolution of the dienes obtained (no plane of symmetry).

The problem to be solved can be seen as to prepare other cyclic olefin metathesis products from a racemic mixture of dienes. The solution of the present demand is the reaction mixture of claim 77.

a- The result of more than 50% ee is achieved by the use of a catalyst (formulae 1a/b-2a/b; fig. 2) having a "sufficient rigidity" and a substrate (tables 3, 5-8) of sufficient reactivity. It is not clear as which catalysts do fall under such a definition. It is questionable if all the possible theoretical catalyst and substrate claimed are solution. This argument is supported by the fact that the substrate 12 (table 5, pg 53) is not: 10% ee. Without restricting the definitions of the two technical features: substrate and catalyst to the examples or generalization thereof, no inventive step could be acknowledged for the composition of claim 77 and methods of preparing it (process by analogy). Every generalisation of the examples, however, would not be allowed under Article 34(2)b) PCT. The claims 1, 3-7, 9-39, 56-66 and 77 do not fulfill the requirements of Article 33(3) PCT.

b- The inventive activity of such "a reaction mixture = composition" as defined in claim 77 is highly questionable.

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**Item VIII**

Certain observations on the international application

1. The expression "a functional substituent" used in claims 15, 21, 26, 30 and 36 is indefinite due to the tremendous theoretical possibilities (Article 6 PCT). The definition given in claim 23 or on page 22 should therefore be introduced in the corresponding claims. The consequence therefrom is that not all those claimed substrates could be solution of the technical problem (Article 33(3) PCT).
2. The term "about" used in claims 6-7, 9-11, 41-55, 67-74, 78 and 80 is vague and leaves the reader in doubt as to the meaning of the technical features to which it refers, thereby rendering the definition of the subject-matters of said claims unclear (Article 6 PCT).
- 2.1 The term "optionally" has no restrictive meaning and the technical feature following such a term is absolutely meaningless (Guidelines CIII-4.6 PCT; see claims 12, 15, 18-21, 23-33, 36-39). If it were to be of any relevance, then it should be reformulate as in a dependent claim.
- 2.2 The passages in the description on page 33 (lines 23-26) and page 56 (lines 1-6) are superfluous (Guidelines CIII-4.3a PCT) and should be deleted.
- 2.3 The following discrepancies between the claims and the description have been noticed:
  - "relative to the amount of substrate" is missing in the description (page 18, line 21) to support claims 9 to 11;
  - the definitions of the substituents M, R<sup>1</sup> and R<sup>2</sup> are missing in claim 84;
  - the optional interruption in the R<sup>4</sup>-R<sup>7</sup> by a functional group as in claim 19 is not supported in the description (page 23, lines 15-23);
  - the structures of the catalyst in claims 85 and 88 are only supported by the figure 2, *i.e.* specific pairing of R<sup>1</sup>-R<sup>3</sup>;
  - the structure of the catalyst in claim 86 is not supported in the figure 2, for R<sup>3</sup> corresponding to *i*-Pr;leading to a doubt concerning the extent of the protection afforded by these claims, thus rendering the claims unclear, contrary to Article 6 PCT. The applicant is requested to remove these inconsistencies, either by amending the claims, or by deleting the embodiment concerned from the description (PCT Guidelines, C-III, 4.3)..